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Patent

Attorney's Docket No. 011900-310

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	
Yoshikatsu KODAMA et al.	Group Art Unit: 1614
Application No.: 09/903,734	Examiner: Vickie Y. Kim
Filed: July 13, 2000	Confirmation No.: 9324
For: PHARMACEUTICAL COMPOSITION USEFUL IN THE PREPARATION OR TREATMENT OF PEPTIC ULCERS	**VIA FACSIMILE TO EXAMINER: (703) 308-2742**

AMENDMENT AND REPLY

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In complete response to the Office Action mailed February 26, 2003, please amend the above-identified application as follows:

In establishing a *prima facie* case of obviousness under 35 U.S.C. § 103, it is incumbent upon the examiner to provide a reason *why* one of ordinary skill in the art would have been led to modify a prior art reference or to combine reference teachings to arrive at the claimed invention. To this end, the requisite motivation must stem from some teaching, suggestion or inference in the prior art as a whole or from the knowledge generally available to one of ordinary skill in the art and not from applicants' disclosure. *See, e.g., Ex parte Nesbit*, 25 U.S.P.Q.2d 1817, 1819 (Bd. Patent Appeals & Interferences 1992). The mere fact that the prior art could be modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. *See, e.g., In re Laskowski*, 10 U.S.P.Q.2d 1397, 1398 (Fed. Cir. 1989). Here, neither EP '032 nor EP '434 teaches or suggests the combination of the claimed IgY antibodies and at least one agent selected from H_2 blockers and proton pump inhibitors.

The antacids disclosed in EP '032 are sodium hydrogencarbonate, magnesium carbonate, precipitated sodium carbonate, and synthetic hydrotalcite. These antacids are clearly distinct from the H_2 blockers and/or proton pump inhibitors used in the present invention. Antacids are generally used for the purpose of neutralizing excess gastric acid. On the contrary, H_2 blockers are an antagonist against histamine H_2 receptor and suppress the secretion of gastric acid. Proton pump inhibitors suppress the secretion of gastric acid by inhibiting H^+, K^+-ATPase (proton pump). Therefore, the functions are different between the antacids disclosed in EP '032 and the H_2 blockers and/or proton pump inhibitors of the present invention. Furthermore, the H_2 blockers and/or proton pump

inhibitors of the present invention are used to treat a different condition or level of gastropathy from that when the antacid is used. Namely, there is no technical common knowledge that these agents are used in the same way.

The antacids disclosed in EP '032 are different in function from the claimed H_2 blockers and/or proton pump inhibitors. Therefore, EP '032, whether taken alone or in combination with EP '434, fails to teach or suggest the claimed invention, as well as the synergistic effects obtained by the claimed combination.

With regard to the teachings of EP '434, the primary active agent (adhesion inhibitor compound) used is mucin, and its mechanism of inhibiting adhesion of Hp to the receptor of gastric mucosa is distinct from that of IgY antibodies used in the present invention as mentioned below. Accordingly, the effects of the combination of IgY antibodies with the H_2 blockers and/or proton pump inhibitors of the present invention cannot be expected from EP '434 (with or without the teachings of '032).

The mucin used in EP '434 is a kind of glycoprotein. The mechanism of the mucin to inhibit the adhesion of Hp to gastric mucosa is that a particular kind of sugar chain in this glycoprotein binds to urease of Hp thereby inhibiting Hp adhesion.

On the contrary, the IgY antibodies used in the present invention are specific antibodies for Hp urease antigen, and bind to urease immunologically by antigen-antibody reaction to form macro aggregates by crossing between antigens (urease) and antibodies, thereby inhibiting adhesion of Hp to gastric mucosa. The use of the inhibitor of gastric acid secretion promotes this process. As a result, the combination of IgY antibodies and

the inhibitor of gastric acid secretion has a remarkable effect of reducing the dose of the antibodies necessary for elimination of Hp. As apparent from Experiment 2 of the present specification, the eradication of Hp can be achieved with a small amount of the antibodies, for example, one-hundredth of the amount of the antibodies required when the antibodies are used alone. The reduction of the dose of the antibodies required is practically a very important advantage, particularly in view of costs.

Thus, the mechanisms of the inhibition of Hp adhesion to gastric musoca are different between the mucin and the antibodies, and therefore the above-mentioned result of the present invention was unexpected.

For at least the reasons set forth above, the combination of EP '032 and EP '434 fails to teach or suggest the claimed invention. Hence, the Examiner is respectfully requested to withdraw this rejection.

Claims 1-4 have also been rejected under the judicially created doctrine of obviousness-type double patenting as purportedly being unpatentable over claims 1-2 and 6 of U.S. patent No. 6,419,926 B2 in view of Kodama (EP 877032 A1 and 1010433 A2). In particular, the Examiner has asserted that the '926 patent discloses an antibody composition using IgY antibodies against Hp urease and a combinatory drug therapy by adding a beneficial additive (e.g., lactic acid bacterium). *See* Official Action at 5. The Examiner has also asserted, based upon the teachings of EP '032 and EP '434, that it would have been obvious to substitute "other beneficial drugs including antacids, inhibitor of gastric